I CLAIM:

1. A method for detecting base changes in a nucleic acid of interest which comprises the following steps:

(a) contacting the nucleic acid of interest with a suitable reference nucleic acid under suitable conditions such that the nucleic acid of interest forms a heteroduplex with the reference nucleic acid;

(b) contacting the heteroduplex with a suitable nuclease or a combination of suitable nucleases so as to selectively cleave the heteroduplex at a position of a base change on the nucleic acid of interest with respect to the reference nucleic acid;

(c) ligating a detectable probe to the cleaved heteroduplex; and

(d) detecting the ligated probe under suitable conditions so as determine the presence and location the base change.

2. The method claim 1 wherein the base change is a single base change.

3. The method claim 1 wherein the nucleic acid of interest is RNA.

4. The method of claim 3 wherein the RNA is expressed from a cDNA library.

5. The method of claims 1 wherein the reference nucleic acid is DNA.

6. The method of claims 1 wherein the reference nucleic acid is a circular nucleic acid.

7. The method of claim 6 wherein the suitable nuclease is S1 nuclease.

8. The method of claim 6 wherein the combination of suitable nucleases is S1 nuclease and RNAase I.

9. The method of claim 1 wherein the detectable probe is a nucleic acid.

10. A kit for detecting base changes in a nucleic acid of interest which comprises the following components:

(a) a suitable reference nucleic acid capable of forming a heteroduplex with the nucleic acid of interest;

(b) a suitable nuclease or a combination of suitable nucleases capable of selectively cleaving the heteroduplex at a position of a base change on the nucleic acid of interest with respect to the suitable reference nucleic acid;

(c) a detectable probe capable of being ligated to the cleaved heteroduplex; and

(d) a means to detect the ligated probe.

11. The kit claim 10 wherein the base change is a single base change.

12. A method for the identification of cancer associated polymorphisms comprising:

(a) preparing at least first, second and third replicas from plates generated by plating a first cDNA library prepared from mRNA from a tumor type from a first patient, said plates containing library clones;

(b) preparing a first probe by

(i) contacting single stranded nucleic acids from a second cDNA library prepared from mRNA from the tumor type from a second patient with complementary single stranded nucleic acids from non-tumor cells of the same tissue type as the tumor type under suitable conditions such that the single stranded nucleic acids from the second cDNA library form heteroduplexes with the complementary single stranded nucleic acids from the non-tumor cells;

(ii) contacting the heteroduplexes with a combination of suitable nucleases so as to selectively cleave the heteroduplex where a base change is present;

(iii) ligating a stuffer sequence to the cleaved heteroduplexes to generate stuffer sequence containing clones;

(iv) generating said first probe selectively from those stuffer sequences containing clones, which first probe comprises nucleic acid sequences corresponding to the single stranded nucleic acids;

(c) repeating step (b) to generate at least a second probe generated from single stranded nucleic acids from a third cDNA library prepared from mRNA from the tumor type from a third patient;

(d) hybridizing said first and second probes to said first and second replicas;

(e) hybridizing the stuffer sequence to said third replica; and

(f) detecting hybridization of said first and second probes to library clones on said first and second replicas and hybridization of said stuffer sequence to library clones on said third replica;

wherein clones that hybridize to the stuffer sequence and to said first and second probes contain cancer associated polymorphisms.

13. The method of claim 12 wherein said first and second probes are RNA probes.

14. The method of claim 12 which further comprises the steps of:

(g) preparing a fourth replica;

(h) preparing a third probe generated from mRNA from single stranded nucleic acids from a fourth cDNA library prepared from mRNA from the tumor type from a fourth patient;

(i) hybridizing said third probe to said fourth replica; and

(j) detecting hybridization of said third probe to library clones on said fourth replica;

wherein library clones that hybridize to the stuffer sequence and to said first, second and third probes contain cancer associated polymorphisms.